IN THE SPECIFICATION

Please replace the paragraph beginning at page 4, line 23 with the following paragraph:

The present invention provides a composition comprising a plurality of cDNAs and their complements which are differentially expressed in ~~brain tissues~~ treated human C3A liver cell cultures and which are selected from SEQ ID NOs: 1-401 as presented in the Sequence Listing. In one embodiment, each cDNA is downregulated at least two-fold, SEQ ID NOs:3, 32, 94, 99, 100, 108, 137, 196, 274, 299, 380; in another embodiment, each cDNA is upregulated at least two-fold, SEQ ID NOs:9, 10, 70, 144, 145, 147, 164, 186, 190, 191, 203, 271, 305, 344. In one aspect, the composition is useful to diagnose a liver disorder selected from hyperlipidemia, hypertension, type II diabetes, and tumors of the liver. In another aspect, the composition is immobilized on a substrate.

IN THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

Please cancel claims 4, 5, 9, and 16-21.

Please amend claim 1 as follows.

Please add new claim 22 as follows.

1. (Currently Amended) A composition comprising a plurality of cDNAs ~~that are differentially expressed in a liver disorder~~ and is selected from SEQ ID NOs:1-5, 7, 9-10, 12-14, 16, 18, 20, 22-26, 28, 30, 32, 34, 36-39, 41, 43-46, 48-49, 51-57, 59-61, 63, 65, 67, 69-72, 74-75, 77, 79-82, 84-85, 87-92, 94, 96-101, 103-104, 106-108, 110-117, 119-120, 122, 124-126, 128-129, 131, 133, 135-137, 139-140, 142, 144-145, 147-148, 150-153, 155-157, 159--162, 164, 166-177, 179, 181-183, 185-186, 188-191, 193-194, 196, 198-199, 201, 203, 205-206, 208, 210-221, 223-224, 226-227, 229-231, 233-234, 236-241, 243-244, 246, 248-257, 259, 261-269, 271, 273-274, 276-277, 279-284, 286-290, 292-295, 297, 299, 301-308, 310, 312, 314-317, 319-323, 325-330, 332, 334-335, 337-342, 344-347, 349-359, 361-366, 368-369, 371-377, 379-389, and 391-401, or their complements.

2. (Original) The composition of claim 1, wherein each of the cDNAs is downregulated at least two-fold and is selected from SEQ ID NOs:3, 32, 94, 99, 100, 108, 137, 196, 274, 299, 380.

3. (Original) The composition of claim 1, wherein each of the cDNAs is upregulated at least two-fold and is selected from SEQ ID NOs:9, 10, 70, 144, 145, 147, 164, 186, 190, 191, 203, 271, 305, 344.

4. (Canceled)

5. (Canceled)

6. (Original) The composition of claim 1, wherein the cDNAs are immobilized on a substrate.

7. (Withdrawn) A high throughput method for detecting differential expression of one or more cDNAs in a sample containing nucleic acids, the method comprising:

(a) hybridizing the substrate of claim 6 with nucleic acids of the sample, thereby forming one or more hybridization complexes;

(b) detecting the hybridization complexes; and

(c) comparing the hybridization complexes with those of a standard, wherein differences between the standard and sample hybridization complexes indicate differential expression of cDNAs in the sample.

8. (Withdrawn) The method of claim 7, where in the nucleic acids of the sample are amplified prior to hybridization.

9. (Canceled)

10. (Withdrawn) A high throughput method of screening a plurality of molecules or compounds to identify a ligand which specifically binds a cDNA, the method comprising:

(a) combining the composition of claim 1 with the plurality of molecules or compounds under conditions to allow specific binding; and

(b) detecting specific binding between each cDNA and at least one molecule or compound, thereby identifying a ligand that specifically binds to each cDNA.

11. (Withdrawn) The method of claim 10 wherein the plurality of molecules or compounds are selected from DNA molecules, RNA molecules, peptide nucleic acid molecules, mimetics, peptides, transcription factors, repressors, and regulatory proteins.

12. (Previously Amended) An isolated cDNA selected from SEQ ID NOs:23, 32, 56, 59, 97, 136, 155, 157, 186, 226, 255, 264, 303, 308, 310, 323, 330, 353, 354, 364, 395.

13. (Original) A vector containing the cDNA of claim 12.

14. (Original) A host cell containing the vector of claim 13.

15. (Withdrawn) A method for producing a protein, the method comprising the steps of:

(a) culturing the host cell of claim 14 under conditions for expression of protein; and

(b) recovering the protein from the host cell culture.

16-21 (Canceled)

22. (New) The method of claim 7, wherein the sample is from liver, and differential expression is diagnostic of hyperlipidemia, hypertension, type II diabetes, or a liver tumor.

REMARKS

The specification has been amended to correct inadvertent typographical and grammatical errors, and the claims have been amended to clarify the invention. The specification has been amended in the paragraph beginning at page 4, line 23 to substitute "treated human C3A liver cell cultures" for "brain tissues" at line 24. Claim 1 has been amended to delete reference to "a liver disorder" in the preamble of the claim. Claims 4 and 5 have furthermore been canceled based on lack of antecedent basis for the term "liver disorder" in claim 1 from which claims 4 and 5 depend. Claim 9 has also been canceled as inadvertently referring to a disease condition not supported by the specification. Claims 16-21 have been canceled as drawn to a non-elected invention. Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications. New claim 22 has been added to recite an additional limitation of the method of claim 7. Support for new claim 22 is found throughout the specification, for example, at page 4, lines 28-30, and at page 18, lines 29-32. No new matter is added by any of these amendments, and entry of the amendments is respectfully requested.

Election/Restriction

The Examiner stated that Applicants election, with traverse, of Group I along with the species of SEQ ID NO:308 and species having SEQ ID NOs:32, 186, and 323 in Paper NOs. 0203 and 0403 respectively are acknowledged. Applicants grounds for traversal were found persuasive, and therefore the four species of nucleic acids having SEQ ID NOs:32, 186, 308 and 323 are hereby being examined. Applicants thank the Examiner for his reconsideration of the Restriction Requirement.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 1-6

The Examiner has rejected claims 1-6 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a was as to enable on skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner stated that, while the specification is enabling for differential expression of an in vitro liver disorder created by captopril and some other drug treatment on human C3A liver cell cultures only, it does not reasonably provide enablement for any liver disorder of any animal. Here, the Examiner stated, the claim is broadly drawn to a method for identifying any liver

disorder in any animal or human species. However, the specification does not provide guidance commensurate in scope with the claim, teaching only one human C3A cell culture study. The specification provides minimal guidance regarding methods for identification of differential expression of DNA in any other liver disorder. There is only one working example of human C3A cell culture study and only a mere recitation in the specification (without working example) that the composition is useful to diagnose a liver disorder selected from hyperlipidemia, hypertension, type II diabetes, and tumors of the liver. It is highly unpredictable whether or what other conservative variations of sequences or what other liver disorder would function.

Applicants Response

Applicants have amended claim 1 to delete reference to the term "liver disorder" and canceled claims 4 and 5. Claims 1-6 therefore no longer recite "any" liver disorder in "any" species. The claimed polynucleotides are fully enabled for use in the diagnosis of specific liver disorders linked to specific drug treatments affecting human liver function, in particular, hyperlipidemia, hypertension, type II diabetes, or liver tumors. The specification, first of all, asserts the use of the human liver C3A cell cultures as a well established in vitro model for human liver tissue at page 1, lines 29-31 of the specification. Secondly, the BACKGROUND of the specification describes various drug treatments in humans and disorders with which such treatments are associated at pages 1-4: e.g., Clofibrate, Fenofibrate---hyperlipidemia; Captopril, Enalapril---hypertension; MCA---liver tumors; and LY294002---type II diabetes. Thirdly, the data in Table 1 and the specification at page 10 presents the results of a microarray study of C3A cell cultures treated with these drugs and showing a pattern of differential expression of the claimed polynucleotides in liver cells that is asserted to provide a diagnostic indicator of the presence of these drugs and hence of the metabolic disorders associated with them. Therefore, the claimed polynucleotides, at least as described in claims 1-6, are fully enabled by the specification as representing genes differentially expressed in human liver cells in response to treatment by the recited drugs, and therefore as diagnostic indicators of the presence of their associated diseases, in particular, hyperlipidemia, hypertension, type II diabetes, or liver tumors. Accordingly, new claim 22 recites an additional limitation of the method of claim 7 in the differential expression of the claimed polynucleotides in liver cells as diagnostic of the presence of hyperlipidemia, hypertension, type II diabetes, or liver tumors.

With these amendments and remarks, applicants submit that claims 1-6, as well as new claim 22, are fully enabled by the specification, and respectfully request withdrawal of the rejection of claims 1-6 under 35 U.S.C. § 112, first paragraph.

Allowable Subject Matter

The Examiner stated that claim 12-14 are allowed in view of the absence of any prior art that either teaches or suggest an isolated cDNA having SEQ ID NOs:32, 186, 308, and 323.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claims 1 and 6, claims 7, 8, 10, 11 and 15 as well as new claim 22, be rejoined and examined as methods of use of the polynucleotides of claims 1 and 6 that depend from and are of the same scope as claims 1 and 6 in accordance with *In re Ochiai* and the MPEP § 821.04

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

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